

Pilot study of cervical cytology screening in a sexually transmitted diseases clinic

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SUMMARY A pilot study of cervical cytology was carried out on 500 new patients at the women's sexually transmitted disease (STD) clinic at this hospital. The aim was to discover the incidence of abnormal smears in order to gauge the worth of cervical cytology as a routine clinic procedure. Information was also gathered on each patient's age, sexual history, method of contraception used, previous smears, and genital infection. Smears showing carcinoma in situ, dysplasia, or warty atypia were regarded as abnormal, and the relevant patients were referred for colposcopy. Seventy three (14.6%) had abnormal smears. Eight women (1.6%), average age 29.7 years, had cervical intraepithelial neoplasia grade III (CIN III) confirmed by histology. One third of the patients with abnormal smears had genital warts, and the incidence of abnormal smears was greater in patients with genital warts than in those without warts. We concluded that STD clinics are useful places in which to carry out cervical cytology screening, and we noted a positive association between infection with genital warts and abnormal smears.

Introduction

Cervical carcinoma may be classified as a sexually transmitted disease (STD) because the oncogenic agent, or agents, appear to be sexually transmissible. All the factors of increased risk are related to coitus, with cervical carcinoma being extremely uncommon in virgin women.¹ Epidemiological evidence suggests that the behavioural factors of increased sexual freedom are related to cervical atypia.^{2,3} The main factors are: first coitus in early adolescence, increased frequency of coitus, multiple sexual partners, and promiscuity in the male partner.^{4,5} Other causative social factors have been suggested: lower socioeconomic status, smoking, poor hygiene, and the use of non-barrier contraception, including the oral contraceptive pill and intrauterine contraceptive devices (IUCDs).⁶ Genital herpes virus,⁷ the papilloma virus,⁸ smegma, trichomonads, and certain proteins of sperm heads^{9,10} have all been suggested as possible carcinogens associated with coitus, and more recent evidence favours the viral infective cause. These sexually transmissible agents are thought to act on the cervix during metaplasia,¹¹

which is most active at puberty, early pregnancy, and during oral contraceptive use.

No other group appears to be more vulnerable (with all the factors of youth, coitus soon after puberty, multiple partners, viral genital infections, and lack of barrier contraception) than the young women who attend STD clinics. They often come from lower socioeconomic groups, are a mobile population, and do not attend general practitioners for regular health checks. In fact, the STD clinic may be their only medical contact.

With these factors in mind, we began a pilot study of cervical cytology in July 1981. During the ensuing 20 months, until March 1983, we screened 500 new patients attending the women's STD clinic. We report a high incidence of cytological abnormality among these patients, and discuss its importance.

Patients and methods

A cervical smear was taken, in conjunction with the routine cervical swabs, from each new patient attending the women's STD clinic. The smear was taken from the squamocolumnar junction with an Ayre's spatula, spread on to a glass slide, fixed, and sent to Christchurch Women's Hospital cytology unit for examination. At this unit, abnormal cytology is reported using the terms dysplasia, carcinoma in situ, or invasive carcinoma, whereas cervical intra-

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epithelial neoplasia (CIN) is reserved for histological diagnosis.

We considered any smears reported as showing warty atypia, dysplasia, or carcinoma in situ to be abnormal. Patients with carcinoma in situ were referred direct for colposcopy. All other abnormal smears were repeated, and the patients were then referred for colposcopy if the abnormality persisted. For the purpose of this study we considered smears reported as showing squamous metaplasia or inflammatory change (due to herpes virus, trichomonas, candida, or actinomycetes) to be normal and did not repeat them.

A questionnaire was added to each patient's notes, recording her age, date of last menstruation, method of contraception used, present infection, age at first intercourse, average number of partners a year, history of infection with herpes, and whether she had previously had a cervical smear.

For comparison, we asked the Christchurch family planning clinic for their cytology screening data for 1982. Their smears were investigated at a private laboratory, but under the supervision of the same pathologist as at Christchurch Women's Hospital.

Results

We took smears from 527 new patients, 27 of whom were excluded from the study as their data were incomplete. In the remaining 500, 200 (40%) of whom had not had a smear taken previously, the average age was 21.96 years. Table I shows that 73 (14.6%) gave abnormal smears; 52 (71%) of these women told us they had had previously normal smear reports.

We referred five patients direct for colposcopy and attempted to repeat the smear on the remaining 68. After vigorous contact tracing and numerous letters and telephone calls 55 (80%) attended. Of these 55, 18 (33%) gave less severe reactions than at first (no abnormality, inflammatory changes, or metaplasia), whereas 28 (50%) gave the same results (atypia or dysplasia), and nine (17%) showed a more severe grade of dysplasia or carcinoma in situ. We also referred these 37 patients for colposcopy; thus 42 patients were referred for colposcopy, 8.4% of the total study population.

Histology of biopsy specimens taken at colposcopy showed (table II) CIN III in eight patients (1.6% of the 500), CIN II in two, condylomata in 17, and metaplasia in five; 10 did not attend for colposcopy. The average age of women with CIN III was 29.7 (range 22-36) years.

With the data on age, sexual history, contraception, and previous smears, we compared our patients who had normal smear results (427) with those who had abnormal smears (73). Among the 27 excluded

TABLE I Results of cervical smears from 500 new patients

	No (%) with results listed
Considered to be normal:	
Normal cervical cells	219 (43.8)
Inflammatory changes	205 (41.0)
Squamous metaplasia	3 (0.6)
Total	427 (85.4)
Considered to be abnormal:	
Warty atypia	40 (8.0)
Mild dysplasia (CIN I)	19 (3.8)
Moderate dysplasia (CIN II)	8 (1.6)
Severe dysplasia (CIN III)	1 (0.2)
Carcinoma in situ	5 (1.0)
Total	73 (14.6)

CIN = cervical intraepithelial neoplasia.

TABLE II Histological results of biopsy specimens taken from 42 patients at colposcopy

	No (% of total study population)
CIN III	8 (1.6)
CIN II	2 (0.4)
CIN I	0
Condyloma accuminatum	17 (3.4)
Squamous metaplasia	5 (1.0)
Patients did not attend	10 (2.0)
Total	42 (8.4)

CIN = cervical intraepithelial neoplasia.

from the study were four who had had more than 100 sexual partners a year (360, 400, 600, and 900 respectively) who we excluded as we thought these patients biased the figures disproportionately. We found it difficult to obtain accurate data on sexual history, with occasional reticence about the questionnaire from both staff and patients. The replies appeared to be influenced by patients' sexual attitudes and anxiety about the initial clinic visit and by the technique of the interviewer. In a few cases, the information altered when the patient was questioned again at subsequent clinic visits.

Table III shows no appreciable differences between the two groups of patients in their age, age at first intercourse, or average number of sexual partners a year. The only method of contraception that showed a significant ($p < 0.05$) difference between the two groups was tubal ligation. This method was used by nine (12.3%) patients with abnormal smears, which contrasted with 21 (4.9%) of those with normal smears. The incidence of past or present infection with herpes virus did not differ appreciably between patients with normal and abnormal smears. Genital warts, however, were found in 48 (11.2%) patients with normal smears compared with 25 (34.3%) of those with abnormal smears, a significant difference ($p < 0.0001$).

TABLE III Comparison between patients with normal and abnormal smears

	No (%) whose smears were:		Difference
	Normal (n = 427)	Abnormal (n = 73)	
Infections diagnosed:			
No infection	161 (37.7)	28 (38.4)	p<0.0001
Genital warts (with or without other infection)	48 (11.2)	24 (34.3)	
Genital herpes (with or without other infection)	17 (4.0)	1 (1.4)	
Miscellaneous infections (gonorrhoea, trichomoniasis, or candidiasis) or having sexual partners with non-specific urethritis, molluscum contagiosum, or <i>Pediculus pubis</i>	201 (47.1)	19 (26.0)	
History of infection with herpes	27 (6.3)	2 (2.7)	
Methods of contraception used:			
Oral contraception	228 (53.4)	36 (49.3)	p<0.05
None	97 (22.7)	10 (13.7)	
Intrauterine device (IUCD)	40 (9.4)	8 (11.0)	
Depo-Provera	22 (5.2)	5 (6.9)	
Tubal ligation	21 (4.9)	9 (12.3)	
Barrier types	19 (4.5)	5 (6.9)	
Other demographic data:			
Mean age of patients (years)	22.0	21.9	
Mean No of sexual partners a year	3.6	5.8	
Mean age at first coitus (years)	16.1	15.9	
No with no smears taken previously	171 (40.1)	21 (28.8)	

We found that 25 (62.5%) of the 40 patients with smears showing warty atypia had not been diagnosed as having genital warts, which indicated that genital warts were not necessarily a simple guide to cervical infection or cytology.

We then looked at the 72 patients with genital warts (table IV) and found that they had a high incidence of abnormal smears (33.3% (24/72)) compared with only 11.5% (49/428) in the patients with no warts, a significant difference ($p<0.0001$). Smears showing warty atypia were found in 20.8% (15/72) of the patients with warts compared with 5.8% (25/428) of those without warts ($p<0.001$). Dysplasia and carcinoma in situ were seen in 12.5% (9/72) of the patients with warts, compared with 5.6% (24/427) in those without warts ($p<0.05$). We thus found our patients with genital warts to have three times the incidence of abnormal smears as in those without warts.

Using our criteria for abnormal smears, we compared our incidence of 14.6% with that of 1.62% from the Christchurch family planning clinic ($p<0.0000001$) (table V). The incidence of carcinoma in situ and invasive carcinoma from the family planning clinic cytology screening was 0.03% compared with 1% in our clinic. These numbers showed that we had nine times their rate of abnormal smears and 33 times their rate of carcinoma in situ, despite their patients being a group of sexually active young women of similar ages as our patients (mean ages of all patients 23.5 v 22 years, mean ages of those with abnormal smears 24.4 v 21.9 years) and from the same city.

A comment must be made on the poor follow up attendance of our patients despite all our efforts. We

TABLE IV Cervical cytology screening in patients with and without genital warts

Histology results	No (%) without warts (428)	No (%) with warts (72)	Difference
Normal smears:			
Normal cervical cells	379 (88.55)	48 (66.67)	
Inflammatory changes			
Squamous metaplasia			
Abnormal smears:			
Warty atypia	25 (5.84)	15 (20.83)	p<0.001
Dysplasia (CIN)	20 (4.67)	8 (11.11)	p<0.05
Carcinoma in situ	4 (0.93)	1 (1.38)	
Total	49 (11.45)	24 (33.33)	p<0.0001

CIN = cervical intraepithelial neoplasia.

TABLE V No (%) of new patients with abnormal smears attending the Christchurch family planning clinic in 1982 and the Christchurch STD clinic in 1981-3

	Family planning clinic (n = 6348)	STD clinic (n = 500)	Difference
Warty atypia	15 (0.24)	40 (8.0)	p<0.0001
Mild dysplasia	66	19	
Moderate dysplasia	13 (1.35)	8 (5.6)	p<0.0001
Severe dysplasia	7	1	
Carcinoma in situ	2 (0.03)	5 (1.0)	p<0.0001
Total	103 (1.62)	73 (14.6)	p<0.0000001

lost 20% of our patients with abnormal smears through non-attendance, and another 25% of our patients who provided repeat smears did not attend for colposcopy. In Christchurch the colposcopy clinic is at Christchurch Women's Hospital. Many of our patients were daunted by the prospect of attending a new hospital and a new clinic and undergoing an unfamiliar examination. Ideally colposcopy or cervicography should be performed on our own clinic premises to retain and reassure these patients.

Discussion

Worldwide epidemiological data show a trend of increasing abnormal smears in young women since the early 1960s, and cervical neoplasia is now considered to be a disease of young women.¹²⁻¹⁴ Whether this is related to the introduction of the oral contraceptive, increasing sexual freedom, the abandonment of barrier contraception, or a combination of these or other factors, is difficult to pinpoint.

In Britain the increased incidence of abnormal cervical smears in younger women was closely followed by increasing mortality from carcinoma of the cervix in young women, despite a general trend of decreasing mortality from carcinoma of the cervix in older age groups.^{15 16} In New Zealand the trends have been identical, with a falling incidence and mortality in women aged over 35 since 1956, but a rise in those aged under 35 since 1959.^{17 18}

The rationale behind cytology screening is the belief that CIN is part of a progressive condition that will lead to invasive carcinoma if left undisturbed, and that detecting and treating the dysplastic or in situ state could prevent invasive carcinoma of the cervix. Mass screening is both costly and time consuming, and there is considerable debate as to its effectiveness. Selective screening of high risk groups is, however, more cost effective. The women who attend STD clinics are not only young and sexually active, but have often experienced first coitus early and have multiple sexual partners, early pregnancy, and genital viral infections, which places them in a high risk category.

Our study confirmed that we are screening patients at very high risk of yielding abnormal smears and that STD clinics are worthwhile places to carry out a screening programme, comparing our figure of 14.6% abnormal smears with the Christchurch family planning clinic's 1.6%. Comparative cytological screening studies of large populations in New Zealand give incidences of 0.2% to 0.5% for dysplasia and carcinoma in situ,^{19 20} compared with our rate of 6.6%. Overseas figures of mass population screening give incidences of abnormal cytology ranging from 0.08% to 2%, varying with age and source,²¹⁻²³ whereas the average incidence on screening by general practitioners appears to be about 0.5%. Selective studies of high risk groups give, as expected, a much higher incidence. A study of a prison population reported that 8.6% had colposcopically proved dysplasias.²⁴

Unfortunately few reports of cytology screening in STD clinics have been published, and we are only aware of six previous reports, five of which were published in the 1950s and 1960s.²⁵⁻²⁹ The two most recent reports came from Birmingham, England, in

1967²⁵ and Seattle, United States, in 1980³⁰ and gave incidences of dysplasia and carcinoma in situ of 6.9% and 11.4% respectively. These figures were both well over five times the incidence of abnormal cytology reported by their countries' national screening programmes.

Many recent studies have discussed the possible role of the herpes simplex virus (HSV) and the human papilloma virus (HPV) in the aetiology of cervical neoplasia either alone or with other carcinogenic agents.^{7 8 31-34} We included data on infection to discover any possible correlation between these viral infections, but could find no appreciable correlation between patients with abnormal smears and those with past or present infection with genital herpes. Concurrent infection with genital warts, however, showed a significant association, occurring in 34% of patients with abnormal smears. One third of the patients with genital warts had an abnormal smear compared with 11.5% of patients with no genital warts, and patients with genital warts had twice the incidence of dysplasia and carcinoma in situ and 3.5 times the rate of warty atypia.

Recent publications have also found that smears showing cervical dysplasia and warty atypia are often associated with HPV without condylomata being visible.^{35 36} In our study 62.5% of our patients with smears showing warty atypia had no visible genital warts. At colposcopy, these patients were often found to have flat, sometimes multiple, lesions with leukoplakia or acetowhite epithelium and a mosaic vessel pattern. These appearances are frequently confused with CIN, and the two conditions can coexist.³⁶

The importance and prevalence of HPV infection of the genital tract affecting the cervix has been underestimated in the past. A study of routine cervical smears from 7281 patients in Sydney showed that 1.3% had evidence of wart virus, while 25% of patients with abnormal smears who were referred for colposcopy had histological evidence of condyloma at punch biopsy, and HPV particles were shown by electron microscopy in 45%.³⁶ Purola and Savia reviewed retrospectively 192 women with genital warts and found koilocytotic atypia in 60% of the cervical smears.³⁷ A more recent study by Walker *et al* of 50 STD clinic patients with genital warts showed that 50% had cytological and colposcopic evidence of infection with cervical wart virus and 36% had changes consistent with CIN I or II.³⁸

The question remains whether HPV has a causative role in carcinogenesis with neoplastic transformation induced virally, or if there is any progression from warty atypia to cervical neoplasia. There is a histological similarity between mild and moderate dysplasia (CIN I and II) and condyloma

acuminatum, and the two conditions can coexist. Shah *et al* found papilloma viral antigens in 50% of patients with mild dysplasia, and that papilloma antiserum stained positively in dysplastic squamous epithelium.³¹ They also found that patients with severe dysplasia and carcinoma in situ and invasive carcinoma gave negative results, which would be consistent with neoplastic transformation induced virally and with the subsequent disappearance of surface viral antigens. They noted that the 50% incidence of HPV antigens was equivalent to that found in cutaneous warts, condylomata accuminata, and oral and laryngeal papilloma, all lesions that are caused by HPV.

HPV appears to be a highly infective sexually transmissible agent. During the 20 month period of our study, the incidence of infection with genital warts rose from 11% to 17% in our women's clinic. In view of this trend, vulval and cervical condylomata and smears showing warty atypia will apparently be an increasing concern. Whether HPV is a causative or promoting agent of cervical carcinoma remains to be proved. It does seem, however, from our study and other research, that women with vulval warts have a high incidence of cervical abnormality and should, as a group, be selectively screened more closely.

In conclusion, our pilot study confirmed that: (1) STD clinics are indeed worthwhile places to conduct cytology screening; (2) this can be performed easily with routine cervical swabs; (3) genital wart infection has a high correlation with abnormal cytology; and (4) consideration should be given to introducing colposcopy or cervicography to STD clinics.

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